

REMARKS

Claims 14-15 and 41-45 are pending and under consideration in the present application. Claims 36 to 42 have been canceled herein without prejudice or disclaimer. Claims 14, 15, 43, and 44 have been amended. Claims 45-50 have been added. Applicants respectfully request entry of the Amendment and reconsideration of the pending claims in view of the remarks and amendments herein. Upon entry of the Amendment, claims 14-15 and 43-50 will be pending and under consideration.

No new matter has been added with the claim amendments or newly added claims. The amendments to claim 14 regarding the defective InaD are supported by claims 15 and 41 as filed and page 30, lines 6-7. The amendment to claim 14 reciting that a difference in detected signal transduction from the first cell and the second cell identifies the test chemical as a modulator of signal transduction, is intended for clarity and is supported, for example; by claims 1 and 41 as filed, as a skilled artisan will recognize from the original claim language that a difference in signal transduction identifies the chemical as a modulator. The amendment to claim 14 indicating that the mutation is not an *inaD*²¹⁵ mutation, is supported by the specification at page 30, lines 6-7.

The amendments to claims 43 and 44 recite the full names for acronyms included in the claims as filed. Newly added claims 45 and 46, which indicate that the amino acid mutation of the defective InaD is in the first (claim 45 only), second, fourth, or fifth PDZ domain, are supported, for example, by the specification at page 29, first full paragraph, which indicates that the invention includes various combinations of PDZ proteins wherein at least one of the PDZ domains is mutated. This section of the specification also supports newly added claim 49, which recites a third cell with a defective InaD having a mutation in a different PDZ domain than the defective InaD of the second cell. Newly added claim 47, which specifies that the amino acid mutation of the defective InaD is an InaD2 or an InaD1 mutation, is supported for example, by figure 2. Newly added claim 48, which recites that the amino acid mutation of the defective InaD is in the third PDZ domain and signal transduction is activated with light and detected by detecting an altered latency period, is supported by page 65, second full paragraph to page 66, first full paragraph. Newly added claim 50 is supported by claims 1 and 42 as filed.

It is acknowledged in the Office Action that claim 41 would be allowable if rewritten in independent form and to overcome the rejection under 35 U.S.C. §112, second paragraph (See Office Action, page 5, second full paragraph). Applicants request clarification regarding this acknowledgement. The Office Action sets out specific allegations in its prior art rejection (see below) for all of the pending claims except claim 42, including a specific allegation regarding claim 41 (page 4, last paragraph). Claim 42 is directed at an InaD polypeptide of SEQ ID NO:1. Attached to the Office Action is a sequence comparison that illustrates that SEQ ID NO:1 of the present application is different than the sequence of InaD in the cited reference, Shieh et al. Therefore, Applicants believe that the Office Action intended to refer to claim 42 in its acknowledgment. Accordingly, claim 42 has been rewritten in independent form as claim 50. Applicants respectfully request allowance of claim 50.

Claim Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 41-45 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action rejects these claims because they recite acronyms. Applicants point out that claim 45 was not pending until entry of the present Response. Therefore, the rejection of claims 41-45 in the prior Office Action, should have been a rejection of claims 41-44. Regarding claims 41-42, the rejection is moot because the claims have been canceled herein, without prejudice. Regarding claims 43-44, all of the acronyms in these claims have been identified by their full name. Accordingly, Applicants respectful request withdrawal of the rejection of claims 41-45 under 35 U.S.C. §112, second paragraph.

Rejection Over Prior Art

Claim Rejections Under 35 U.S.C. §102

Claims 14, 15, 41, and 43-45 stand rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Shieh et al. (*Neuron* 14:201-210 (1995)). To anticipate an invention, each and every element of a claim must be found in a single prior art reference. MPEP §2131; *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628,631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Furthermore, to anticipate and invention under 35 U.S.C. §102, a prior art reference must contain an 'enabling disclosure'... ." MPEP §2121.01; and In re Hoeksema, 399 F.2d 269, 158 USPQ 596 (CCPA 1968).

The Office Action alleges that Shieh et al. teach a phototransduction model system for G-protein coupled signal transduction that is encompassed by the methods of the rejected claims. The Office Action alleges specifically that Shieh et al. teach a method for identifying modulators of signal transduction related to phototransduction, by contacting a first cell such as a photoreceptor cell, with calcium, wherein the cell includes more than one signal transport protein, and wherein the cell comprises a polynucleotide that encodes an InaD transducisome. Furthermore, the Office Action alleges that Shieh et al. teach a second cell identical to the first cell except that the second cell includes an InaD^{p215} mutant. Finally, the Office Action asserts that Shieh et al. teach activating signal transduction in the first cell and second cell with light induced currents and detecting and comparing signal transduction detected by whole cell patch clamp recordings.

The invention of pending claim 14, from which the remaining rejected claims depend, recites a method for identifying a modulator of signal transduction by contacting a first cell and a second cell with a test chemical. The first cell includes a signal transduction protein and InaD. The second cell includes a polynucleotide encoding a defective InaD wherein the defective InaD includes an amino acid mutation in a PDZ domain, other than an *inaD*²¹⁵ mutation. The method includes activating and detecting signal transduction of the first cell and the second cell, and comparing this signal transduction between the first and second cell.

Shieh et al. are silent as to a method that includes a defective InaD having a mutation in a PDZ domain, other than an *inaD*²¹⁵ mutation. Although in their sequence characterization, Shieh et al. mention that InaD includes 2, 40 amino acid regions that share sequence similarity with various other proteins (Shieh et al., page 202, last sentence to page 203, second sentence), Shieh et al. provide no data to suggest that these regions provide a function for InaD. Furthermore, although the 2, 40 amino acid repeats mentioned in Shieh et al. are within the first and third PDZ regions identified in the present invention, the repeats mentioned by Shieh et al. do not correspond precisely to any of the PDZ domains identified in the present application. The

repeats mentioned in Shieh et al. extend from amino acid 47 to 87, and from amino acid 389 to 429 (Figure 2). The present application identifies InaD PDZ domains as extending from amino acids 13 to 107, 245 to 333, 362 to 449, 485 to 577, and 580 to 665. Finally, the *inaD*²¹⁵ mutation does not fall within the repeats mentioned by Shieh et al. Therefore, Shieh et al. do not suggest that mutants of the repeats may effect signal transduction. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 14, 15, 41, and 43-45 stand rejected under 35 U.S.C. §102(b).

Claims 45-50 recite additional features that further distinguish these claimed inventions over Shieh et al. Newly added claim 45 recites that the amino acid mutation of the defective InaD is in the first, second, fourth, or fifth PDZ domain. Newly added claim 46 recites that the amino acid mutation of the defective InaD is in the second, fourth, or fifth PDZ domain. As identified by the present application, the *inaD*²¹⁵ mutant is a missense mutation in the third PDZ domain. As indicated above, Shieh et al. mention 2, 40 amino acid repeats that fall within the first and third PDZ domain, but are silent as to repeats that fall within the other PDZ domains. Newly added claim 47, recites that the defective InaD is an *inaD*² or an *inaD*¹ mutation, which are not mentioned by Shui et al.

Claim 48 recites that the amino acid mutation of the defective InaD is in the third PDZ domain and signal transduction is activated with light and detected by detecting an altered latency period. Shui et al. mention that InaD²¹⁵ mutants show a slow deactivation, but are silent that slow deactivation is caused by an altered latency period. The present application identifies that the slow activation was surprisingly not due to a defect in deactivation or feedback regulation, but rather as the result of latency times between stimulus and quantum bump generation. (Page 65, last paragraph to page 66, first paragraph).

Claim 49 recites contacting a third cell with the test chemical, wherein the third cell comprises a polynucleotide encoding a defective InaD that includes a mutation in a different PDZ domain than the mutant InaD of the second cell. Shieh et al. is silent regarding a third cell because, *inter alia*, Shieh et al. does not identify InaD mutations other than InaD^{P215}. Finally, as mentioned above, claim 50 is based on previously pending claim 42, directed at an InaD of SEQ

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Zuker et al.

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ID NO:1 as the InaD of the first cell. As illustrated in the sequence comparison attached to the Office Action, entitled "us-09-462-517-1.rspt," the InaD of SEQ ID NO:1 has a different amino acid sequence than the InaD of Shieh et al.

In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

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